REMARKS

The Examiner suggests that claims 1, 2 and 4-14 are pending in the instant application. Applicants believe that claims 1, 2, 4-14 and 21-32 are pending in the instant application. Claims 1, 2 and 4-14 have been rejected. Claims 21-32 have been canceled as they depend from a claim that was canceled in the previous reply. Claim 1 has been amended. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Election/Restriction

Applicants acknowledge that the Restriction Requirement wherein Applicants have elected SEQ ID NO: 3 has been deemed proper and made Final.

II. Rejection of Claims Under 35 U.S.C. 103(a)

Claims 1, 2 and 4-14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Ding et al., Peresleni et al., and Lousson-Wood et al., in view of Nunokawa et al. (US Patent 6,203,982) and Monia et al. (US Patent 5,872,242). The Examiner suggests it would have been *prima facie* obvious for one of skill to

make and use antisense compounds to iNOS RNA based on the teachings of Ding et al., Peresleni et al., and Leesoon-Wood et al., and further because these references teach implication of iNOS in pathological conditions and the benefits of inhibiting expression of iNOS, while Nunokawa wt al. disclose SEQ ID NO: 3 and Monia et al. teach modifications of antisense. Applicants respectfully traverse this rejection.

At the outset, the claims have been amended to refer to specific nucleobase regions within the sequence of human iNOS to be targeted by antisense compounds. Support for these amendments to the claims can be found throughout the specification as filed but in particular at pages 78-81, Table 1.

Ding et al. (1996) disclose only one antisense compound targeted to bases 1-21 of the translation initiation site of mouse iNOS mRNA. No other target regions are taught or suggested by this paper, including any nucleobase regions within SEQ ID NO: 3.

Peresleni et al. (1996) teach antisense compounds targeted to nucleotides 85-82 of human iNOS cDNA that is referred to by GenBank accession number L24553 (see page 5972). The authors claim this region of that sequence corresponds to the 5'-UTR, the initiation codon, and two codons from the open-reading frame of iNOS cDNA. No

other target regions of the gene are taught or suggested. Moreover, this paper fails to teach the target nucleobase regions of the instant invention as now claimed.

Leesoon-Wood et al. (1996) is an abstract with few details provided. The abstract does disclose the preparation of 6 antisense oligonucleotides, 15 mer each, that corresponded to different parts of the coding region of an iNOS. However, the exact sequence of this iNOS and the target regions within the coding region of this iNOS are not taught or suggested. In addition, no other target sites on the gene are taught or suggested. Therefore, this paper fails to teach the regions of iNOS RNA that are recited in the amended claims.

Therefore, either alone or when combined, the primary references cited by the Examiner fail to teach the limitations of the amended claims. The secondary references cited fail to overcome the deficiencies in teaching of those primary references.

Monia et al. teach modifications of antisense oligonucleotides in general. However, nowhere does this patent teach or suggest antisense compounds of any type targeted to any region of the human iNOS RNA. Therefore, this secondary reference fails to overcome the deficiencies in teaching of the primary references.

Nunokawa et al. (US Patent 6,203,982) disclose the sequence of human iNOS (SEQ ID NO: 3) and methods for screening for compounds that regulate expression of this gene. However, nowhere does this paper teach or suggest nucleobase regions within this gene that can be successfully targeted by antisense compounds as claimed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as amended, which claim antisense compounds targeted to specific nucleobase regions of iNOS RNA (SEQ ID NO: 3), and thus cannot render the instant claimed invention obvious. It is only with the specification in hand that one of skill would understand which nucleobase regions could be successfully targeted with antisense compounds. The combination of art provides no motivation nor an expectation of success at targeting the specific regions as now claimed. Therefore, this

combination of prior art cannot render the instant invention obvious. Withdrawal of this rejection is therefore respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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